Oregon Health & Science University
School of Medicine

Scholarly Projects Final Report

Title *(Must match poster title; include key words in the title to improve electronic search capabilities.)*

Standardizing the workup of Biliary Atresia: the utility of stool color, HIDA scans, and IR percutaneous cholangiograms

Student Investigator's Name

Alexandra Stendahl

Date of Submission *(mm/dd/yyyy)*

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Project Course *(Indicate whether the project was conducted in the Scholarly Projects Curriculum; Physician Scientist Experience; Combined Degree Program [MD/MPH, MD/PhD]; or other course.)*

Scholarly Project Curriculum

Co-Investigators *(Names, departments; institution if not OHSU)*

Mentor's Name

Henry Lin, MD

Mentor's Department

Pediatric Gastroenterology

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Concentration Lead's Name

Ladawna Gievers, MD

Project/Research Question

What is the predictive value of HIDA scan's in diagnosing obstructive cholestasis in the neonate at OHSU? Goal to understand how a HIDA scan factors into the diagnostic work-up for neonatal cholestasis and specifically biliary atresia.

Type of Project *(Best description of your project; e.g., research study, quality improvement project, engineering project, etc.)*

Research Study

Key words *(4-10 words describing key aspects of your project)*

Biliary atresia, HIDA scan, percutaneous cholangiogram, stool color, neonatal cholestasis

Meeting Presentations

If your project was presented at a meeting besides the OHSU Capstone, please provide the meeting(s) name, location, date, and presentation format below (poster vs. podium presentation or other).

OHSU SOM Research Forum, May 2025
Oregon Academy of Family Physicians Conference, June 2025

Publications *(Abstract, article, other)*

If your project was published, please provide reference(s) below in JAMA style.

Submission to Archive

Final reports will be archived in a central library to benefit other students and colleagues. Describe any restrictions below (e.g., hold until publication of article on a specific date).

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Next Steps

What are possible next steps that would build upon the results of this project? Could any data or tools resulting from the project have the potential to be used to answer new research questions by future medical students?

Doing a QI project on the implementation of a standardized procedure between GI and surgery to reduce time to OR and reduce number of diagnostic tests before diagnosis.

Scholarly Project Final Report

Report*: Information in the report should be consistent with the poster, but could include additional material. Insert text in the following sections targeting 1500-3000 words overall; include key figures and tables. Use Calibri 11-point font, single spaced and 1-inch margin; follow JAMA style conventions as detailed in the full instructions.*

Introduction *(≥250 words)*

Biliary Atresia is a rare neonatal liver disease that is the leading cause of liver-related death among children, as well as major contributor to pediatric liver transplants[1]. Surgical treatments include the Kasai hepatoportoenterostomy, however early diagnosis of the disease is critical, as delayed intervention leads to worse outcomes. The ideal timeframe for surgical intervention is before 60 days of life, with the ideal target of 45 days of life[1].

Prompt evaluation of cholestasis in neonates is essential, especially those with conjugated hyperbilirubinemia (serum conjugated bilirubin concentration greater than 1.0 mg/dL)[2]. Neonatal cholestasis can be caused by a variety of factors including obstructive causes such as biliary atresia, biliary cysts, and tumors, as well as neonatal sclerosing cholangitis, hepatitis, inherited cholestatic disorders, and genetic abnormalities affecting bile synthesis[2]. These should be considered when biliary atresia is on the differential.

Evaluation of biliary atresia is done as quickly as possible to ensure the patient reaches the operating room before 60 days of life. Kasai surgeries done prior to 60 days of life (ideally 45) have much better outcomes than those performed later. Survival rates with native liver increased as age at operation decreased, with the best survival <30 days of age, showing a clear benefit for intervention as early as possible[3]. Even with the Kasai surgery, one study found that 63% of patients still required a liver transplant, and half of those within a year of the Kasai surgery[4].

There are many useful tests in identifying or ruling out biliary atresia, from imaging exams like ultrasound, HIDA scans, and IR percutaneous cholangiograms, to serologic and pathologic markers such as liver biopsies, and matrix metalloproteinase-7 (MMP-7)[5-9]. Table 1 shows sensitivities and specificities of various tests, as found in literature review. The combination of tests that a physician may use to diagnose biliary atresia differs greatly and can depend on age of child, medical comorbidities, and diagnosing physician.

Imaging tests are frequently performed, both at OHSU and elsewhere. Ultrasounds are a quick way to exclude other anatomic causes of cholestasis and evaluate anatomy and can be helpful in narrowing down diagnosis, as well as potentially positively identify biliary atresia[10,11]. More specifically, the absence or irregular shape of a gall bladder on ultrasound can help positively identify biliary atresia[12]. Additional features characteristic of biliary atresia such as the triangular cord sign can be seen if detailed ultrasonographic protocol is used, with the triangular cord sign having a specificity of 0.95 and sensitivity of 0.68[12]. HIDA scans can help rule in or rule out biliary atresia, as lack of excretion of the tracer can be indicative of biliary atresia. Radiological research suggests the use of phenobarbital in HIDA scans, however that adds a 5-day incubation time, which gastroenterologists are not keen to do due to the time pressure in diagnosing biliary atresia. Newer interventional radiology guided cholangiograms are useful in identifying biliary duct architecture.

Liver biopsy is a useful tool to histologically view changes consistent with obstruction, such as expanded portal tracts, portal tract edema, fibrosis and inflammation[13]. Biopsies are also highly helpful in the diagnosis of biliary atresia, with an estimated sensitivity of 90.1%[14]. Timing can play a role in biliary atresia identification from liver biopsies, as one study notes biopsies done too early can result in false negatives[15].

Test	Sensitivity	Specificity	Source
HIDA	98%	70%	Kianifar et al. 2013
IR Percutaneous Cholangiogram	100%	87%	Zhang et al. 2024
MMP7	91%	84%	Zhang et al. 2024
GGT	81%	72%	Zhang et al. 2024
Ultrasound triangular cord	85%	97%	Yoon et al. 2017
Liver biopsy	91%	93%	Lee et al. 2016

Table 1: Sensitivity and Specificity as identified by literature review.

Patient education has also played an important role in the identification of rare diseases. In Taiwan and Canada, programs were instituted to give new parents stool color cards to allow parents to identify the pale colored stool characteristic of biliary atresia. In both countries, after the institution of color cards, biliary atresia outcomes improved significantly, suggesting that patient education plays a key role in the identification of possible patients and quick workup[1,15].

HIDA scans are often part of the workup for OHSU patients presenting with neonatal cholestasis, however wait times for HIDA scans can be multiple days-weeks and may or may not be useful in diagnosing biliary atresia. Due to the urgent matter of getting an infant in for surgery once biliary atresia has been diagnosed, waiting multiple days for an inconclusive test is not an ideal workflow. This study evaluated the utility of HIDA scans, including sensitivity and specificity at OHSU. Because there is known variance in diagnostic testing between individual providers, and between surgical and medical providers. Provider input through surveys was additionally collected to understand what tests would comprise an expedited, complete work up of biliary atresia prior to surgical intervention. From this information, recommendations of useful diagnostic tests were created to be implemented at OHSU

Methods *(≥250 words)*

Retrospective Chart Review

This study conducted a retrospective cohort analysis of infants <1 year who underwent HIDA scans for neonatal cholestasis from January 2013 to December 2023, as well as infants who underwent Kasai surgery during that same period. Data collected included patient history, age, medical comorbidities, mention of stool color in the chart, history of cholestasis, diagnostic work up including imaging tests, HIDA scans including whether premedication with phenobarbital was performed, IR percutaneous cholangiograms, relevant serologic tests, liver biopsy details, surgical dates and outcomes were all recorded.
Time from identification of cholestasis to surgical intervention was calculated for those who ultimately underwent Kasai surgery. HIDA scan sensitivity, specificity, positive predictive value, and negative predictive value were all calculated.

Provider Survey

Seven pediatric surgeons at OHSU were surveyed. They were presented with the following case: “Consider a 27-day old with cholestasis (total bilirubin 4.5, conjugated bilirubin 2.3, GGT 432) and the following workup” and presented with the following work up scenarios.

1. Positive IR percutaneous cholangiogram & positive liver biopsy
2. Positive IR percutaneous cholangiogram
3. Positive liver biopsy

4. Positive ultrasound & positive HIDA scan
5. Positive ultrasound & positive liver biopsy
6. Positive HIDA scan
7. Positive IR percutaneous cholangiogram & *negative* HIDA
8. Positive ultrasound & elevated MMP7
9. Positive ultrasound & positive liver biopsy & *negative* HIDA
10. Positive ultrasound & elevated MMP7 & negative HIDA

Each surgeon then marked whether each work up scenario would prompt them to proceed to the operating room for an intra-operative cholangiogram and possible Kasai surgery. Surgeons also provided comments on tests and scenarios if desired. Survey results were analyzed based on the number of surgeons that would proceed to the operating room. Comments were collated and used in identifying challenges for particular tests.

Results *(≥500 words)*

58 patients were scheduled to undergo HIDA scans, with 46 completing the scan. Of those, nine were diagnosed with biliary atresia and underwent Kasai surgery. Based on the 46 completed HIDA scans, HIDA scans demonstrated a specificity of 72% and a sensitivity of 100%, with a positive predictive value of 47% and negative predictive value of 100% (Figure 1).

20 infants were diagnosed with Biliary Atresia during the study duration and taken to the operating room for a Kasai procedure. Time from initial presentation to surgery ranged from 3 days to 70 days, with the average time to surgery 19.25 days and the median 15 days. All but 1 case was performed within 38 days of presentation.

Stool color had a sensitivity of 50% and a specificity of 32%. It was assessed in 50 patients (Figure 2). Stool color was described as “acholic”, “clay colored”, or “pale” ten times in the chart, however had low correlation with ultimate diagnosis. Additionally, vocabulary seemed to be used interchangeably within the same note and the same provider. Stool photos, when included in the chart, ranged anywhere from a true pale yellow/grey to brighter yellow and brown.

Provider surgeon survey had seven respondents. All were pediatric surgeons at OHSU. Surgeons were asked which diagnostic scenario would result in a child being taken to the operating room without any further work up. All seven surgeons would proceed to the operating room with the combination of a positive percutaneous cholangiogram with interventional radiology and a positive liver biopsy. Fewer (4) surgeons would proceed to the operating room with only a positive biopsy, or only a positive percutaneous cholangiogram, noting that they would want additional correlating data before proceeding. Three surgeons would proceed with a positive HIDA scan and positive ultrasound, or positive ultrasound and positive liver biopsy, noting that these tests were less conclusive, that they may want a percutaneous cholangiogram, or that it would depend on the age of the child. No surgeon would proceed with just a positive ultrasound & elevated MMP7, noting that MMP7 were fairly new tests and they were unsure of the diagnostic utility. Two surgeons would consider operating with a positive IR percutaneous cholangiogram & negative HIDA, though they note that they would check the quality of both tests, as negative HIDA scans were typically definitive for excluding biliary atresia. No surgeons would operate with a positive ultrasound & positive liver biopsy & negative HIDA, again noting the high sensitivity of HIDA scans in ruling out biliary atresia.

	BA	Not BA	
Not excreted (+)	9	10	PPV = 47%
Excreted (-)	0	27	NPV = 100%
	Sen. 100%	Spec. 72%	

Figure 1: HIDA scan sensitivity and specificity table.

	BA	Not BA	
Acholic (+)	5	27	PPV = 15%
Normal or not mentioned (-)	5	13	NPV = 72%
	Sen. 50%	Spec. 32%	

Figure 2: Stool color scan sensitivity and specificity table.

Table 1: Pediatric surgeon survey of diagnostic test preference.

Case: Consider a 27-day old with cholestasis (total bilirubin 4.5, conjugated bilirubin 2.3, GGT 432) and the following workup:		
Diagnostic Workup	# of surgeons who would operate without further workup	Comments if would need further workup prior to surgery
Positive IR percutaneous cholangiogram & positive liver biopsy	7/7	
Positive IR percutaneous cholangiogram	4/7	May want additional supporting data
Positive liver biopsy	4/7	Would want a cholangiogram
Positive ultrasound & positive HIDA scan	3/7	HIDA not sufficient Prefer an IR percutaneous cholangiogram May depend on patient age

Positive ultrasound & positive liver biopsy	3/7	May depend on patient age Would prefer IR percutaneous cholangiogram
Positive HIDA scan	2/7	Would want a cholangiogram or liver biopsy
Positive IR percutaneous cholangiogram & negative HIDA	2/7	Negative HIDA fairly definitive Diagnostic uncertainty > more workup May recommend biopsy
Positive ultrasound & elevated MMP7	0/7	Not much experience with using MMP7 Would want biopsy data or IR percutaneous cholangiogram before surgery
Positive ultrasound & positive liver biopsy & negative HIDA	0/7	Negative HIDA fairly definitive Confirm HIDA is good quality Recommend IR percutaneous cholangiogram
Positive ultrasound & elevated MMP7 & negative HIDA	0/7	Confirm HIDA is good quality Likely get biopsy or IR percutaneous cholangiogram

Discussion *(≥500 words)*

This study reviewed the use of HIDA scans in the diagnosis of biliary atresia, the utility of stool color in diagnosing biliary atresia, and evaluated surgeon preference for diagnostic work up.

Although HIDA scans are not considered the gold standard test, they are still often used in the diagnostic work up of Biliary Atresia at OHSU. Because of Biliary Atresia's time sensitive nature (surgical intervention before 60 days of life, ideally 45), spending 5 days premedicating with phenobarbital in order to perform a HIDA scan is a significant delay. Therefore evaluating the utility and re-evaluating the appropriateness of their use given advances in other diagnostic procedures is warranted.

We found that HIDA scans at OHSU had 100% sensitivity and 72% specificity, which is similar to the values reported in the literature (98% sensitivity and 70% specificity), and therefore would be useful as a test to rule out Biliary Atresia more than a rule-in diagnostic tool. This was demonstrated in the survey where surgeons valued negative HIDA scans and except for extenuating circumstances, would be comfortable ruling out Biliary Atresia at that point. However, they typically wanted additional corroborating evidence when the HIDA scan was positive, indicating that although positive HIDAs are 70% sensitive, that is not enough for a surgeon to justify the risks of a surgical intervention in an infant. In the instances where a HIDA scan differed from other clinical evidence, surgeons commented that the quality of the HIDA scan must be evaluated, and that they may pursue additional testing at that time.

The imaging test that surgeons valued more, is a newer test: the percutaneous cholangiogram performed by interventional radiology, especially in concert with a liver biopsy, which can be obtained in

the same procedure. Surgeon's had much higher confidence in these tests, which is reflected in the literature, where percutaneous cholangiograms are reported to have sensitivity of 100% and specificity of 87%, and liver biopsies have sensitivity of 91% and specificity of 93%.

Surgeons did not have as high of confidence in newer serologic testing such as MMP7 and GGT, despite sensitivities and specificities in the literature similar to other common diagnostic tests (MMP7 sensitivity 91%, specificity 84; GGT sensitivity 81%, specificity 72%). One surgeon reported that it is not commonly part of their inpatient workflow yet, and weren't as familiar with the test. Another noted that, depending on hospital, these could be send-out tests which may take days or weeks to return, which is unhelpful in an urgent work up.

Stool color can be a helpful warning sign to educate parents about, however hyperbilirubinemia does not always correlate with a change in stool color, and changes in stool color have a wide differential. Educational stool color cards have had moderate success in catching cases of biliary atresia when tested abroad and likely have value in being an easy-to-identify trigger for a parent or a care team in the NICU.

Given this data, we recommend the following action items: 1) in centers with IR teams, a percutaneous cholangiogram and liver biopsy should be the primary diagnostic step when working up neonatal cholestasis. 2) HIDA scans should only be used when cholangiograms are not available and should be primarily considered a test to rule out biliary atresia. The care team should carefully weigh the cost of 5 days of premedication and should evaluate any simultaneous diagnostic testing they may want, should the test be positive. 3) Centers should increase the use of serologic tests like MMP7 and GGT *when available in a timely manner,* as serologic tests are easy to obtain and have high sensitivity and specificity. 4) It may be useful for surgeon and medicine teams to collaborate on a shared diagnostic work up, as there was significant variation in preferred tests between surgical and medical services, and within the specialties as well. While having high confidence in a diagnosis is important, eliminating unnecessary testing likely will expediate the time-to-surgery, reduce the cost, and expose a neonate to less risk involved with invasive procedures.

Conclusions *(2-3 summary sentences)*

This study demonstrated that HIDA scans have high sensitivity but lower specificity and while they may work well as rule-out tests, they are not as helpful as ruling in.

Surgeons prefer percutaneous cholangiograms in combination with liver biopsies, which can be done during a single procedure with the IR team.

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